

Dr. Roger Walk

July 12, 2003

Dear Dr. Walk,

Thank you for your time and for sharing your knowledge with me on July 11.

You were absolutely right about the number of tobacco related carcinogens; "over 60" applies to both human and animal carcinogens.

Enclosed are the papers (references) supporting genetic link with smoking-related lung cancer..

1. Polymorphism at codon 72 (Arg/Pro) of the common tumor suppressor gene p53 and susceptibility to smoke-induced lung adenocarcinoma:

Fan R, Wu MT, Miller D, Wain JC, Kelsey KT, Wiencke JK, Christiani DC. The p53 codon 72 polymorphism and lung cancer risk. *Cancer Epidemiol Biomarkers Prev.* 2000;9:1037-42.

Kawajiri K, Nakachi K, Imai K, Watanabe J, Hayashi S. Germ line polymorphisms of p53 and CYP1A1 genes involved in human lung cancer. *Carcinogenesis* 1993;14:1085-9.

2. p53 mutation carriers and an increased risk for smoking related lung cancer:

Hwang SJ, Cheng LS, Lozano G, Amos CI, Gu X, Strong LC. Lung cancer risk in germline p53 mutation carriers: association between an inherited cancer predisposition, cigarette smoking, and cancer risk. *Hum Genet* 2003 Jun 11 [Epub ahead of print]

3. Homozygous GMSP1 deletion (glutathione-S-transferase) and smoking-related lung cancer in Japanese population:

Kihara M, Kihara M, Noda K. Lung cancer risk of GSTM1 null genotype is dependent on the extent of tobacco smoke exposure. *Carcinogenesis* 1994;15:415-8.

Kihara M, Noda K, Kihara M. Distribution of GSTM1 null genotype in relation to gender, age and smoking status in Japanese lung cancer patients. *Pharmacogenetics*. 1995;5 Spec No:S74-9.

Association of GMSP1 deletion and non-small lung cancer in female smokers in the US:

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Tang DL, Rundle A, Warburton D, Santella RM, Tsai WY, Chiampasert S, Hsu YZ, Perera FP. Associations between both genetic and environmental biomarkers and lung cancer: evidence of a greater risk of lung cancer in women smokers. *Carcinogenesis* 1998;19:1949-53.

4. Combination of GSTM1(-) and CYP1A1(m2/m2) and susceptibility to smoking-related cancers in Japanese:

Kihara M, Kihara M, Noda K. Risk of smoking for squamous and small cell carcinomas of the lung modulated by combinations of CYP1A1 and GSTM1 gene polymorphisms in a Japanese population. *Carcinogenesis*. 1995;16:2331-6.

Combined GSTM1 null/GSTP1 Val genotype and lung cancer in former smokers:

Perera FP, Mooney LA, Stampfer M, Phillips DH, Bell DA, Rundle A, Cho S, Tsai WY, Ma J, Blackwood A, Tang D; Physicians' Health Cohort Study. Associations between carcinogen-DNA damage, glutathione S-transferase genotypes, and risk of lung cancer in the prospective Physicians' Health Cohort Study. *Carcinogenesis* 2002;23:1641-6.

There are, of course, several studies which disagree with these data, especially meta-analysis studies. However, in pooled analysis studies the authors combine different ethnic groups and, most importantly, different gene polymorphism detection methods, anything from simple PCR to RFLP/PCR to southern blot analysis to sequencing. This, I believe, should not be done.

These are just my thoughts. I am a new person to the field of tobacco hazards and any comments/ feedback will be highly appreciated.

Thanks again for everything.

Sincerely,
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